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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/034,621	12/21/2001	**Walter Callen**	D1350-6US	9848

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	

MAIL DATE	DELIVERY MODE
06/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/034,621	CALLEN ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9-12,16,28-44,46-49,51-53 and 55* is/are pending in the application.

4a) Of the above claim(s) *34,35,38 and 44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-11,28-33,36,37,39-43,46-49,51-53 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The appeal filed on 7/5/2007 is defective. As per MPEP 1204 [R-3] < Notice of Appeal 35 U.S.C. 134. Appeal to the Board of Patent Appeals and Interferences, which states

> >Applicant cannot file an appeal in a continuing application, or after filing a request for continued examination (RCE) under 37 CFR 1.114, until the application is under a rejection. Accordingly, applicant cannot file a notice of appeal with an RCE regardless of whether the application has been twice rejected prior to the filing of the RCE.

Accordingly the instant action is in response to applicants previously filed request for continuation.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/2/2007 has been entered.

Applicant's amendment of claim 12, in the paper of 7/2/2007, is acknowledged. Claims 1-7, 9-12, 16, 28-44, 46-49, 51-53 and 55 are still at issue and are present for examination.

Applicants' arguments filed on 6/26/2007 and 7/2/2007 have been fully considered and are deemed to be persuasive to overcome some of the /rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claims 34, 35, 38 and 44 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Objections

Claim 51 is objected to because of the following informalities: Claim 51 recites "an enzymatically active fragment of (a)," however "(a)" does not exist. It is noted that applicants previously inserted "(a)" in the claims submitted on 10/16/2007, however this amendment has apparently been deleted in the current claim set.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 9-11, 28-33, 36, 37, 39-43, 46-49, 51-53 and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for nucleic acid comprising SEQ ID NO: 1 and encoding a polypeptide having polymerase activity, does not reasonably provide enablement for any nucleic acid comprising a sequence that encodes a polypeptide having polymerase activity wherein the sequence comprises a mere 100 consecutive bases of the sequence set forth in SEQ ID NO: 1.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 1, 2, 4-7, 9-12, 28-33, 36, 37, 39-43, 46-49, 51-53 and 55. In response to this previous rejection, applicants have amended claim 12 and traverse the rejection as it applies to the newly amended claims. Claim 3 is included in this rejection on the basis that claim 3 is drawn to "a" sequence as set forth in SEQ ID NO: 1 and this includes fragments of SEQ ID NO: 1, rather than "the" sequence as set forth in SEQ ID NO: 1.

Applicants continue to traverse this rejection as previously on the basis that the specification enabled the skilled artisan at the time of the invention to identify, and make and use, the genus of nucleic acids encoding polypeptides having polymerase activity, including nucleic acids having at least 95% sequence identity to SEQ ID NO: 1. Applicants maintain that the specification did provide the skilled artisan with a reasonable amount of guidance with respect to production of and screening for nucleic acids with at least 95% sequence identity to SEQ ID NO: 1 which encode polypeptides having polymerase activity.

Applicants continue to submit that they have addressed this issue in their previous responses in, inter alia, an expert declaration where Dr. Short declared that the state of the art at the time of the invention and the level of skill of the person of ordinary skill in the art for screening enzymes for polymerase activity was very high. Applicants

submit that Dr. Short declared that it would not have been necessary for the skilled artisan to understand which specific regions of the polymerase sequence or structure needed to be modified without affecting function or activity to routinely generate the genus of polypeptides used in the claimed methods, as Dr. Short declared that methods for making and screening sequence modifications and enzyme fragments were sufficiently comprehensive, routine and predictable at the time of the invention to predictably generate polymerase-encoding sequences without need of knowing which specific regions of a sequence or structure affected function or activity. Applicants submit that Dr. Short declared that methods known at the time of the invention for modifying nucleic acid and polypeptide sequences in combination with high through-put enzyme (polymerase) screening known at the time of the invention, made methods that require previous knowledge of protein structure, including secondary or tertiary structure, active site sequences, and the like obsolete and unnecessary.

Applicants also noted that if one skilled in the art desired some structural guidance as to what amino acid substitutions could be made to make the genus of polymerase-encoding nucleic acids of the invention, such guidance could be found both in the specification and the state of the art at the time of the invention.

Applicants submit that accordingly, the specification did provide guidance as to what base and residue changes could be made to make the genus of polymerase-encoding nucleic acids of the invention, as one skilled in the art would be able to predict which specific regions of polymerase structure could be modified to generate a polymerase with a desired activity without undue experimentation), that information was,

inter alia, readily available in the form of polymerase sequences known in the art at the time of the invention. Applicants argue that routine, simple sequence alignment comparison of known polymerase sequences would have identified regions of identity and dissimilarity to provide guidance to the skilled artisan as to which sequences could be changed, or not changed, to generate structural and/or functional variations of an exemplary polymerase of the invention.

Furthermore, Applicants respectfully aver that if desired direction and guidance to the skilled artisan as to which base (and amino acid residues) may be modified to obtain a structural or functional polymerase variant was also readily available in the art at the time of the invention. For example, the three dimension structure of polymerases had been described, see, e.g., Wang (1997) Cell 89(7): 1087-1099; Eom (1995) Acta Crystallogr. D. Biol. Crystallogr. 5 l(Pt 6): 1086-1088, thus providing direction as to which amino acid residues can be modified and how structure correlates with function. Furthermore, at the time of the invention one of skill in the art would have been aware of the many studies of polymerase activity and active sites, see, e.g., Blasco (1993) J. Biol. Chem. 268(22): 16763-16770, "Phi 29 DNA polymerase active site"; Blasco (1995) J. Biol. Chem. 270(6):2735-2740, "Primer terminus stabilization at the phi 29 DNA polymerase active site. Mutational analysis of conserved motif KXY"; de Vega (1997) J. Mol. Biol. 270(1):65-78, "An invariant lysine residue is involved in catalysis at the 3'-5' exonuclease active site of eukaryotic-type DNA polymerases."

Applicants submit that one skilled in the art at the time of the invention had many sources of guidance, in addition to the specification, to determine which bases (amino

acid residues) of a sequence of the invention could be modified to make, identify, screen for and use structural and/or functional variants of an exemplary polymerase of the invention without undue experimentation.

Applicants submit that 35 USC § 112 varies with a number of factors including the predictability of the art and the breadth of the claims. *In re Wands',* 858 F.2d 731,736-37, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). In general, the stringency of the enablement requirement increases with the unpredictability of the art. *In re Fisher,* 427 F.2d 833,839, 166 USPQ (BNA) 18, 24 (CCPA 1970). However, even in an unpredictable art, "applicants are not required to disclose every species encompassed by their claims," *In re Vaeck,* 947 F.2d 488,496, 20 USPQ2d (BNA) 1438, 1445 (Fed. Cir. 1991) (citing *In re Angstadt,* 537 F.2d 498,502-03, 190 USPQ (BNA) 214, 218 (CCPA 1976)), but the disclosure must be sufficient to teach one skilled in the art "how to make and.., use the invention as broadly as it is claimed." *Id.* And, the scope of enablement need only present a reasonable correlation to the scope of the claims. *See e.g., In re Fisher,* 427 F.2d 833,839, 166 USPQ 18, 24 (CCPA 1970). Nevertheless, not everything necessary to practice the invention need be disclosed, what is well-known may be omitted. *See In re Buchner,* 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991).

Accordingly, Applicants respectfully submit that amended claims are fully enabled by and described in the specification to overcome the rejection based upon 35 U.S.C. § 112, first paragraph.

Applicant's complete argument is acknowledged and has been carefully considered, however is not found persuasive for the reasons previously made of record and repeated herein.

Applicants continued traversal is on the basis that applicants specification enabled the skilled artisan at the time of the invention to identify, and make and use, the genus of nucleic acids encoding polypeptides having polymerase activity, including nucleic acids having at least 95% sequence identity to SEQ ID NO: 1. Applicants maintain that the specification did provide the skilled artisan with a reasonable amount of guidance with respect to production of and screening for nucleic acids with at least 95% sequence identity to SEQ ID NO: 1 which encode polypeptides having polymerase activity and applicants present the declaration by Dr Short as well as case law supporting applicants position.

The basis of the maintenance of the rejection is that contrary to applicants argument, applicants claims are not merely limited to (a) those nucleic acids which have at least 95% sequence identity to SEQ ID NO: 1 and encode a polypeptide with polymerase activity, but rather applicants claims are so broad that they are drawn to "(b) an enzymatically active fragment of (a)", which literally continues to be drawn to an enzymatically active fragment of a nucleic acid. It is believed that applicant's intent is to refer to a nucleic acid which encodes a polypeptide which is an enzymatically active fragment of the polypeptide encoded by (a), which for the purpose of the current rejection continues to be so broad as not requiring "polymerase activity". The maintenance of this rejection is considered appropriate as the polypeptides encoded by

those nucleic acids which have 95% sequence identity to the SEQ ID NO: 1 encompass a great many enzymatic activities in addition to polymerase activity. At the very least polymerases themselves comprise polymerase activity, 3'-5' exonuclease activity, 5'-3' exonuclease activity, nucleotide binding activity and template binding activity.

It is suggested that an amendment clarifying that the encoded polypeptide has polymerase activity would be helpful in overcoming the current rejection.

Additionally a number of applicants claims, such as claim 3, recite “a sequence as set forth in SEQ ID NO: 1” which for is interpreted as encompassing fragments of SEQ ID NO: 1, not just SEQ ID NO: 1. Applicants might correct this by an amendment such as the replacement of "a" with "the.

Additionally a number of applicants claims such as claim 3, recite “or sequences fully complementary thereto” which could be improved such as “or sequences fully complementary to the full-length of ” so that it is clear that the claimed complement is a complement of the full-length nucleic acid(i.e. SEQ ID NO: 1).

Because of this lack of guidance, and the extended experimentation that would be required to determine which substitutions would be acceptable to retain the desired enzymatic activity and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides of the claimed genus defined merely as all nucleic acids having at

the claimed identity to SEQ ID NO: 1 and encoding a polypeptide having any enzymatic activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including those nucleic acids comprising a sequence which encodes a polypeptide which has any enzymatic activity of the encoded amino acid sequence. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those nucleic acids having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Rgh
5/28/2008

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652